

August 21, 2012 Tanaka Precious Metals Tanaka Holdings Co., Ltd.

"Development of Embolic Coils Using a Non-magnetic Alloy" by Tanaka Precious Metals and Others to be Adopted in a Project Commissioned by the Ministry of Economy, Trade and Industry

With Kyoto University and Maruho Hatsujyo Kogyo, Developing the World's First Embolic Coil Not Causing Metal Artifacts in MRI Scans, Aiming for Release to the Market within 2017

Tanaka Kikinzoku Kogyo K.K.^(*1) (a company of Tanaka Precious Metals, Head office: Chiyoda-ku, Tokyo; President & CEO: Hideya Okamoto) today announced that the "Embolic Coils Using a Non-magnetic Alloy" jointly developed with Professor Hiroo Iwata and Research Fellow Tomonobu Kodama of the Kyoto University Institute for Frontier Medical Sciences and Maruho Hatsujyo Kogyo Co., Ltd. (Head office: Kyoto-shi, Kyoto; President & CEO: Yasunobu Oku) has been selected as a candidate for use in the "2012 Project to Develop Medical Equipment and Devices to Solve Unmet Medical Needs"^(*2) commissioned by the Ministry of Economy, Trade and Industry.

After the consignment agreement is concluded and the project is settled upon, a grant will be received from the national government from this fiscal year, and <u>development of the world's first</u> <u>non-magnetic embolic coil for cerebral aneurysms that does not cause metal artifacts^(*3) in MRI^(*4)</u> (magnetic resonance imaging) devices will commence, aiming for release into the market within <u>2017.</u>

In recent years, endovascular treatment techniques^(*5) including coil embolization of aneurysm have continued to make remarkable progress. However, new problems have arisen with the spread of such technologies, and because metal artifacts are caused by conventional metal coils, this has been a significant problem affecting the direction of treatment.

In order to address such issues, this commissioned project will involve the joint development of a non-magnetic embolization coil that limits the occurrence of metal artifacts significantly better than existing products, and enables MRI scans to be performed after endovascular treatment. During the development, Tanaka Kikinzoku Kogyo will evaluate the process of metal formation and processing, Kyoto University will perform magnetic evaluation and evaluate the MRI images, and Maruho Hatsujyo Kogyo will perform technical development of coil processing.

In joint research conducted to date, the results of the educational research on "research and development of devices for minimally invasive treatment" performed from FY2009 to FY2011 by JST Innovation Plaza Kyoto (Kyoto-shi, Kyoto) include the successful development of a non-magnetic metal based on a platinum-gold alloy expected to have high biological affinity and mechanical characteristics. In future commissioned development, efforts will be made to evaluate the process of metal formation and processing, perform magnetic evaluation, evaluate the MRI images, and process coils.

The Impact of Metal Artifacts

A treatment method called endovascular embolization is widely used to treat ruptured cerebral aneurysms, which are a type of stroke^(*6), by inserting a coil into the aneurysm. However, it has been indicated that there are many cases in which repeat treatment is required or subsequent bleeding occurs due to the regrowth of the residual aneurysm after endovascular embolization has occurred, and it is necessary to continue evaluating the status of the embolization by performing regular imaging scans after treatment.

Until now, imaging tests were performed using CT angiography, but this is a test in which a catheter is inserted into a blood vessel, and involves risk because the test itself is invasive^(*7). To address this, it has become more common to perform angiography using MRI, which is a technology making remarkable progress, enabling imaging tests that are non-invasive and can be repeated more easily than the conventional method.

However, because metal artifacts are produced by embolization coils in MRI scans, parts of normal parent vessels (normal blood vessels where an aneurysm has occurred) are not visualized (see Photo 1), and residual aneurysms in which the coil has not been completely inserted appear to be embolized with no blood flow. When parent vessels appear constricted due to metal artifacts, it is difficult to determined whether the coil mass has deviated from the aneurysm, or whether the clotting in the embolized aneurysm has spread to normal blood vessels. Furthermore, there is also a possibility of underestimating the probability of repeat treatment if residual aneurysms are not visualized.

<Photo 1: Comparison of angiography and MRI images>

A part where there is no constriction in the angiogram (left photo) appears to be a constricted blood vessel due to an artifact around the conventional metal coil (A).





Angiogram

MRI image

From educational research by JST Innovation Plaza Kyoto on "research and development of devices for minimally invasive treatment" (FY2009 to FY2011)

Backdrop to the Research

Over 300,000 patients^(*8) in Japan's aging society experience strokes each year, and this number is increasing. Although the mortality rate is in decline, it is the most common cause of being confined to bed, and has a significant impact on the growing cost of social security in Japan when subsequent care is also factored in.

In recent years, there has been a rapid increase in endovascular treatment as an effective method for treating strokes. Endovascular surgery is less invasive than conventional means of surgery, and because it is able to reach areas that are difficult to reach in conventional craniotomy procedures ^(*9), there has been a rapid increase in cases and significant advances are expected to be made in the future alongside the development of new medical equipment. Furthermore, although endovascular treatment performed using a variety of radiological imaging is common, patients' exposure to radiation cannot be avoided, and it is desirable to make the transition to performing endovascular treatment using MRIs in the future.

In order to respond to such medical needs, Tanaka Kikinzoku Kogyo, Kyoto University and Maruho Hatsujyo Kogyo are conducting research and development and clinical trials of an "Aneurysm Embolization Coil Using a Non-magnetic Alloy" and will work to move toward its practical application in medical devices.

(*1) Tanaka Kikinzoku Kogyo K.K.

The core company conducting manufacturing operations in the Tanaka Precious Metals Group, which has Tanaka Holdings Co., Ltd. as its holding company

- (*2) Project to Develop Medical Equipment and Devices to Solve Unmet Medical Needs A project carried out by the Ministry of Economy, Trade and Industry with the aim of promoting the development and improvement of medical equipment and other related equipment that can contribute to solving unmet medical needs by utilizing that manufacturing capabilities of small and medium companies and other industries.
- (*3) Metal artifact

Distortion of an image that occurs when there is metal inside the body when performing an MRI.

(*4) MRI

A device that utilizes magnetic resonance imaging to visualize information on the body.

(*5) Endovascular treatment technique

A method for treating intracranial sites of pathology from inside blood vessels that is primarily performed by inserting a catheter into the femoral artery. Its use has rapidly become widespread in recent years due to its low invasiveness and safety.

(*6) Stroke

One of the three most common causes of death among Japanese (cancer, heart attack, stroke). It includes cerebral infarction, cerebral hemorrhage and subarachnoidal hemorrhage (ruptured cerebral aneurysm). In recent years, the mortality rate has declined with advances in medical technology, but it is the most common cause of being confined to bed, and much money is spent on medical expenses.

(*7) Invasive

This refers to the possibility that surgery, administration of drugs or tests are harmful to the patient's body.

(*8) Reported in "Research on evaluation of the quality of the cerebral apoplexy medical treatment using the regional crisis registration of cerebral apoplexy" (Lead researcher: Kazuo Suzuki), a comprehensive research project on health science commissioned under Health Labour Sciences Research Grant.

(*9) Conventional craniotomy procedures

Surgery involving the cutting the scalp and removal of part of the cranial bone. A microscope is used from the open part to directly squeeze the base of the aneurysm with a clip.

■Tanaka Holdings Co., Ltd. (Holding company of Tanaka Precious Metals)

Headquarters: 22F, Tokyo Building, 2-7-3 Marunouchi, Chiyoda-ku, Tokyo Representative: Hideya Okamoto, President & CEO Founded: 1885 Incorporated: 1918 Capital: 500 million yen Employees in consolidated group: 3,456 (FY2010) Net sales of consolidated group: 891.0 billion yen (FY2010) Main businesses of the group: Manufacture, sales, import and export of precious metals (platinum, gold, silver, and others) and

various types of industrial precious metals products. Recycling and refining of precious metals. Website: http://www.tanaka.co.jp/english

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Headquarters: 22F, Tokyo Building, 2-7-3 Marunouchi, Chiyoda-ku, Tokyo Representative: Hideya Okamoto, President & CEO Founded: 1885 Incorporated: 1918 Capital: 500 million yen Employees: 1,532 (FY2010) Sales: 865.4 billion yen (FY2010) Businesses: Manufacture, sales, import and export of precious metals (platinum, gold, silver, and others) and various

Manufacture, sales, import and export of precious metals (platinum, gold, silver, and others) and various types of industrial precious metals products. Recycling and refining of precious metals. Website: <u>http://pro.tanaka.co.jp/en</u>

<About the Tanaka Precious Metals>

Established in 1885, the Tanaka Precious Metals has built a diversified range of business activities focused on the use of precious metals. On April 1, 2010, the group was reorganized with Tanaka Holdings Co., Ltd. as the holding company (parent company) of the Tanaka Precious Metals. In addition to strengthening corporate governance, the company aims to improve overall service to customers by ensuring efficient management and dynamic execution of operations. Tanaka Precious Metals is committed, as a specialist corporate entity, to providing a diverse range of products through cooperation among group companies.

Tanaka Precious Metals is in the top class in Japan in terms of the volume of precious metal handled, and for many years the group has developed and stably supplied industrial precious metals, in addition to providing accessories and savings commodities utilizing precious metals. As precious metal professionals, the Group will continue to contribute to enriching people's lives in the future.

The eight core companies in the Tanaka Precious Metals are as follows.

- Tanaka Holdings Co., Ltd. (pure holding company) Tanaka Kikinzoku Kogyo K.K.
- Tanaka Kikinzoku Hanbai K.K.
- Tanaka Denshi Kogyo K.K.
 Tanaka Kikinzoku Jewelry K.K.

- Tanaka Kikinzoku International K.K.
- Electroplating Engineers of Japan, Limited
- Tanaka Kikinzoku Business Service K.K.

Kyoto University Institute for Frontier Medical Sciences

Location: 53 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto-shi, Kyoto Representative: Hiroo Iwata, Director, Institute for Frontier Medical Sciences Established: 1998

Content of research: Development of devices for cerebrovascular treatment, analysis of interaction between artificial pancreases, artificial materials and the body.

Website: http://www.frontier.kyoto-u.ac.jp/

Maruho Hatsujyo Kogyo Co., Ltd.

Head office: 21, Yawatacho, Nishishichijo, Shimogyo-ku, Kyoto-shi, Kyoto Representative: Yasunobu Oku, President & CEO Established: 1954 Capital: 93.6 million yen Employees: 230 (as of FY2011) Sales: 6.5 billion yen (FY2011) Business content: 1. Manufacture and sale of various precision springs and leaf springs

2. Design, manufacture and sale of various automated packing devices and energy-saving devices Website: <u>https://www.maruho-htj.co.jp/</u>